

Electrocardiographic ST-segment monitoring during controlled occlusion of coronary arteries^{☆,☆☆}

Andreas Haeberlin, MD,^{a,b} Evelyn Studer, BM,^{a,b} Thomas Niederhauser, MSc,^{b,c} Michael Stoller, MD,^a Thanks Marisa, MSc,^{b,c} Josef Goette, PhD,^c Marcel Jacomet, PhD,^c Tobias Traupe, MD,^a Christian Seiler, MD,^a Rolf Vogel, MD, PhD^{d,*}

^aDepartment of Cardiology, Bern University Hospital, Bern, Switzerland

^bARTORG Center for Biomedical Engineering, University of Bern, Bern, Switzerland

^cInstitute of Human Centered Engineering, Bern University of Applied Sciences, Bern, Switzerland

^dDepartment of Cardiology, Bürgerspital Solothurn, Solothurn, Switzerland

Abstract

Background: Ischemia monitoring cannot always be performed by 12-lead ECG. Hence, the individual performance of the ECG leads is crucial. No experimental data on the ECG's specificity for transient ischemia exist.

Methods: In 45 patients a 19-lead ECG was registered during a 1-minute balloon occlusion of a coronary artery (left anterior descending artery [LAD], right coronary artery [RCA] or left circumflex artery [LCX]). ST-segment shifts and sensitivity/specificity of the leads were measured.

Results: During LAD occlusion, **V3 showed maximal ST-segment elevation** (0.26 mV [IQR 0.16–0.33 mV], $p = 0.001$) and sensitivity/specificity (88% and 80%). During RCA occlusion, **III showed maximal ST-elevation** (0.2 mV [IQR 0.09–0.26 mV], $p = 0.004$), aVF had the best sensitivity/specificity (85% and 68%). During LCX occlusion, **V6 showed maximal ST-segment elevation** (0.04 mV [IQR 0.02–0.14 mV], $p = 0.005$), and sensitivity/specificity was (31%/92%) but could be improved (63%/72%) using an optimized cut-off for ischemia.

Conclusion: **V3, aVF and V6 show the best performance to detect transient ischemia.**

© 2014 Elsevier Inc. All rights reserved.

Keywords:

ECG; ST-segment monitoring; Coronary occlusion

Introduction

Continuous electrocardiographic ST-segment monitoring has shown to be useful for the detection of transient myocardial ischemia during and after percutaneous coronary interventions or surgery [1,2]. Transient myocardial ischemia may occur without overt symptoms and remain clinically silent. However, ischemic episodes detected by ST-segment monitoring are associated with poor patient outcome [3].

To diagnose transient ischemic episodes in time, electrocardiographic ST-segment monitoring is performed.

Although ischemia is detected best by a standard 12-lead ECG [1,4], continuous ECG monitoring during coronary angiography or on the intensive care unit is often done with a reduced three-lead system only [5]. The reason is that a standard 12-lead ECG requires 10 electrodes and cables placed at the body surface. This may interfere with patient care. In addition, critically ill patients are often restless which impairs continuous 12-lead ECG registration. Thus, to trade off reliable ischemia detection against patient comfort, the most sensitive and specific ECG leads for ischemia detection have to be identified. This allows to select appropriately the most valuable leads for ST-segment monitoring.

In the past, several authors have investigated the performance of different ECG leads for ST-segment monitoring [5–11]. All these studies, however, have major limitations. Prospective data about specificity of the different ECG leads for ischemia detection are lacking and quantitative coronary collateral flow measurements were not performed [5–11]. Many studies lack controlled ischemia

[☆] Disclosures: None.

^{☆☆} Financial support: This work was funded by the Commission for Technology and Innovation, Switzerland; the Department of Cardiology, Bern University Hospital, Switzerland, and the Swiss Heart Foundation.

* Corresponding author. Bürgerspital Solothurn, 4500 Solothurn, Switzerland.

E-mail address: rolf.vogel@spital.so.ch

induction [5,6,9,10] and an intracoronary lead or quantitative reporting about ST-segment changes during ischemia [5–7,9,10]. Therefore, only limited data about the performance of the different ECG leads are available [1,4].

The goal of this study was to quantify prospectively ST-segment changes in 19 different ECG leads in a well-controlled experimental setting. Using an intracoronary lead as reference, we aimed to quantify the performance of the 12 standard leads, V7–V9, V3R, V4R and an esophageal lead.

Methods

Study design

For this prospective observational single center study, we included 45 patients referred for coronary angiography due to suspected or known coronary artery disease. We excluded patients with acute coronary syndrome, uncontrolled hypertension and severe valvular heart disease. In addition, patients with bundle branch block or significant Q-waves in the surface ECG leads were excluded.

All patients underwent coronary angiography with simultaneous ECG registration during a 1-minute balloon occlusion of a coronary artery (either the left anterior descending artery [LAD], the right coronary artery [RCA] or the left circumflex artery [LCX]).

Patients without coronary artery disease (CAD) were randomly assigned to one of those three groups, until a group reached 15 patients. Subsequently, the patients were randomized to the remaining groups. In case of single-vessel disease, patients underwent percutaneous coronary intervention of the target vessel, including the 1-minute balloon occlusion. In case of two- or three-vessel disease and more than one vessel should have been treated, the first vessel undergoing percutaneous coronary intervention was used for the measurements.

The study was approved by the local ethics committee and patients gave informed consent.

Coronary angiography and collateral flow measurement

Patients underwent left heart catheterization via the right femoral artery. Central venous pressure (CVP) was measured via the right femoral vein. During low-inflation pressure balloon occlusion in the proximal coronary artery, the recruitable collateral flow relative to the normal flow through the non-occluded coronary artery was measured (CFI) [12]. Pressure-derived CFI was calculated by simultaneous measurement of the mean aortic pressure (P_{ao}), distal coronary occlusion pressure (P_{occ}) and CVP ($CFI = (P_{occ} - CVP)/(P_{ao} - CVP)$). We measured P_{occ} using a pressure wire (PressureWire Certus®, St. Jude Medical, USA).

ECG acquisition

During coronary angiography, patients underwent 19-channel ECG registration including the standard leads, V3R, V4R, V7, V8, V9, an intracoronary ECG (icECG) and an esophageal ECG (eECG).

For icECG registration, the proximal end of the pressure wire was connected to the ECG recorder by an alligator clamp. The icECG detects myocardial ischemia with high sensitivity [13]. An ST-segment elevation of ≥ 0.1 mV at the j-point was considered as a sign for myocardial ischemia.

The eECG was recorded using a hexapolar esophageal catheter (Esosoft®, FIAB, Italy), which was connected to the ECG recorder. We recorded a bipolar esophageal ECG using electrodes 2 and 6 with 60-mm interelectrode spacing. The signal was registered at the site of the maximal ventricular signal amplitude as assessed visually. The standard leads were registered using a conventional ECG recorder (AT-104 PC®, Schiller AG, Baar, Switzerland). V3R, V4R, V7–V9, the eECG and icECG were recorded using a dedicated biosignal monitor (BioRadio®, Cleveland Inc., USA). The precordial leads and the icECG were measured against an average reference (Wilson's Central Terminal with electrodes on both arms and on the left leg, connected through a 5-k Ω resistor.)

ECG analysis

ECG analysis was performed using custom-made software based on MATLAB® (MathWorks, USA). All ECG channels underwent low-pass filtering (35Hz) to remove high-frequency noise (powerline interference and muscle tremor). No high-pass filters were applied. Heartbeats were averaged over 20-second intervals using an R-wave-triggered template matching [14] to attenuate signal fluctuations particularly observed in the icECG and eECG. Beats were aligned on the R-wave peak. For each 20-second interval, the relative ST-segment shift at the j-point was measured (compared to baseline, i.e. the non-occluded vessel). The j-point was determined manually by a physician for each averaged ECG lead. Changes in ST-segment amplitude were analyzed for all leads separately and considered to be indicative for ischemia if reaching the threshold according to the AHA/ACCF/HRS recommendations [15]. Since these recommendations do not provide a threshold value for the eECG, an ST-segment elevation/depression of ≥ 0.1 mV at the j-point was considered to be indicative for ischemia.

The sensitivity of an ECG lead to detect myocardial ischemia was calculated by dividing the number of the “ECG leads showing ischemia” by the number of all “true myocardial ischemias” during coronary occlusion. An “ECG lead showing ischemia” was defined to show ST-segment elevation according to the AHA/ACCF/HRS recommendations and simultaneous ST-segment elevation of ≥ 0.1 mV at the j-point in icECG. We defined a “true myocardial ischemia” if ST-segment elevation of ≥ 0.1 mV at the j-point in the icECG was observed.

The specificity of an ECG lead to detect myocardial ischemia was calculated by dividing the number of the “ECG leads showing no ischemia” by the number of all “true non-ischemic ECG's” during coronary occlusion. An “ECG lead showing no ischemia” was defined to show ST-segment elevation less than the AHA/ACCF/HRS threshold without a simultaneous ST-segment elevation of ≥ 0.1 mV at the j-

point in iECG. We defined a “true non-ischemic ECG’s” if no ST-segment elevation of ≥ 0.1 mV at the j-point in the iECG was observed.

To calculate sensitivity/specificity for reduced lead combinations, we retrospectively evaluated whether any lead of the combination showed signs of ischemia. If at least one lead showed ischemic signs, the lead combination was considered to have successfully detected an ischemic event (logical OR).

Statistical analysis

For statistical analysis R version 2.15.1 for Windows was used [16]. Patient baseline characteristics are expressed as median and interquartile range (IQR). For comparison of categorical variables, Fisher’s exact test was used. Continuous variables were compared using a Kruskal–Wallis test after assessing the data for normal distribution. ST-segment shifts of the different ECG leads were compared using a Wilcoxon signed rank test with Bonferroni–Holm adjustment for multiple testing. Receiver operating characteristics (ROC) analysis was performed to assess sensitivity and specificity of the ECG leads. Areas under the ROC curve and corresponding 95% confidence intervals (CI) were reported. For pair-wise comparison of ROC curves, a DeLong test was performed. For descriptive correlation analysis of CFI and ST-segment shifts, Spearman rank correlation coefficients were calculated. A p -value ≤ 0.05 was considered significant.

Results

Population characteristics

There were no differences between the three patient groups regarding age, gender, cardiovascular risk factors or medication (Table 1). In addition, no differences with respect to number of diseased vessels, CFI, blood chemistry and echocardiographic parameters were found (Table 2).

Table 1

Baseline patient characteristics for the three groups undergoing temporary occlusion of the LAD, RCA or LCX.

	LAD (n = 15)	RCA (n = 15)	LCX (n = 15)	P
Age (years)	68 \pm 8	66 \pm 8	65 \pm 9	0.36
Male gender (%)	12 (80)	12 (80)	12 (80)	1
Arterial hypertension (%)	8 (53)	9 (60)	9 (60)	1
BMI (kg/m ²)	26 \pm 4	28 \pm 5	28 \pm 6	0.61
Diabetes (%)	5 (33)	2 (13)	5 (33)	0.41
Dyslipidemia (%)	9 (60)	11 (73)	5 (33)	0.11
Smoking, current or former (%)	9 (60)	11 (73)	6 (40)	0.22
Family history for coronary artery disease (%)	3 (20)	6 (40)	5 (33)	0.61
Acetylsalicylic acid (%)	12 (80)	10 (67)	12 (80)	0.75
β -Blockers (%)	8 (53)	6 (40)	9 (60)	0.65
ACE inhibitors (%)	4 (27)	5 (33)	6 (40)	0.92
Statins (%)	10 (67)	11 (73)	12 (80)	0.91
Diuretics (%)	2 (13)	3 (20)	4 (27)	0.89
Nitrates (%)	3 (20)	1 (7)	2 (13)	0.86

Table 2

Coronary angiographic, echocardiographic and laboratory data for the three groups undergoing temporary occlusion of the LAD, RCA or LCX.

	LAD (n = 15)	RCA (n = 15)	LCX (n = 15)	P
Number of diseased vessels				0.31
0 (%)	0 (0)	1 (7)	3 (20)	
1 (%)	4 (27)	5 (33)	1 (7)	
2 (%)	4 (27)	2 (13)	5 (33)	
3 (%)	7 (47)	7 (47)	6 (40)	
CFI (dimensionless)	0.11 \pm 0.08	0.10 \pm 0.07	0.13 \pm 0.06	0.29
ST-segment elevation ≥ 0.1 mV in iECG after 60-s occlusion (%)	15 (100)	11 (73)	12 (80)	0.13
No symptoms during coronary occlusion (%)	3 (20)	8 (53)	3 (20)	0.10
LVEF (%)	58 \pm 6	62 \pm 6	53 \pm 16	0.28
LVEDD (mm)	53 \pm 6	49 \pm 8	44 \pm 4	0.20
Hemoglobin (g/l)	138 \pm 10	138 \pm 16	137 \pm 20	1
Creatinine (μ mol/l)	83 \pm 14	88 \pm 41	83 \pm 18	0.86
Heart rate (beats/minute)	68 \pm 16	69 \pm 11	68 \pm 15	0.97

ST-segment shifts during transient ischemia

Fig. 1 summarizes the ST-segment changes after the 60-second balloon occlusion to induce ischemia in the territories of the LAD, RCA or LCX, i.e. the three patient groups. Fig. 2 shows a representative ECG example of the most sensitive lead for each occlusion territory.

Detection of ischemia in the LAD territory

Median intracoronary ST-segment elevation was 1.63 mV (IQR 0.94–2.4 mV). Among the other leads, median ST-segment elevation was most pronounced in lead V2 (0.21 mV [IQR 0.12–0.25 mV]), V3 (0.26 mV [IQR 0.16–0.33 mV]) and V4 (0.22 mV [IQR 0.13–0.28 mV]). ST-segment shifts were statistically significant in V3R and V1–V5 (all $p \leq 0.015$, Fig. 1, top panel). ST-segment elevation was larger in lead V3 compared to lead V3R, V1 and V5 (all $p \leq 0.003$).

These ST-segment shifts result in a high sensitivity and specificity of the precordial leads (Fig. 3, top panel). V3 had a sensitivity/specificity of 88%/80% (AUC 0.85 [CI 0.73–0.98]) to detect ischemia in the LAD territory (using the AHA/ACC/HRS thresholds [15]). V4 showed 55%/95% sensitivity/specificity (AUC 0.9 [CI 0.81–0.99]). Sensitivity and specificity of V3 were higher than in lead I, II, aVL, V6 and V7 (all $p \leq 0.029$).

Detection of ischemia in the RCA territory

Median intracoronary ST-segment elevation was 0.23 mV (IQR 0.09–0.45 mV). In the other leads, median ST-segment elevation was most pronounced in lead III (0.2 mV [IQR 0.09–0.26 mV]), aVF (0.17 mV [IQR 0.07–0.24 mV]) and eECG (0.15 mV [IQR 0.08–0.19 mV]). ST-segment shifts were statistically significant in I, II, III, aVR, aVL, aVF, V4R, V2 and the eECG (all $p \leq 0.013$, Fig. 1, middle panel). Among these leads, ST-segment shift was more prominent in aVF compared to lead I and V4R (both $p \leq 0.021$).

Sensitivity and specificity of aVF to detect ischemia in the RCA territory were 85% and 68%, respectively (AUC 0.77

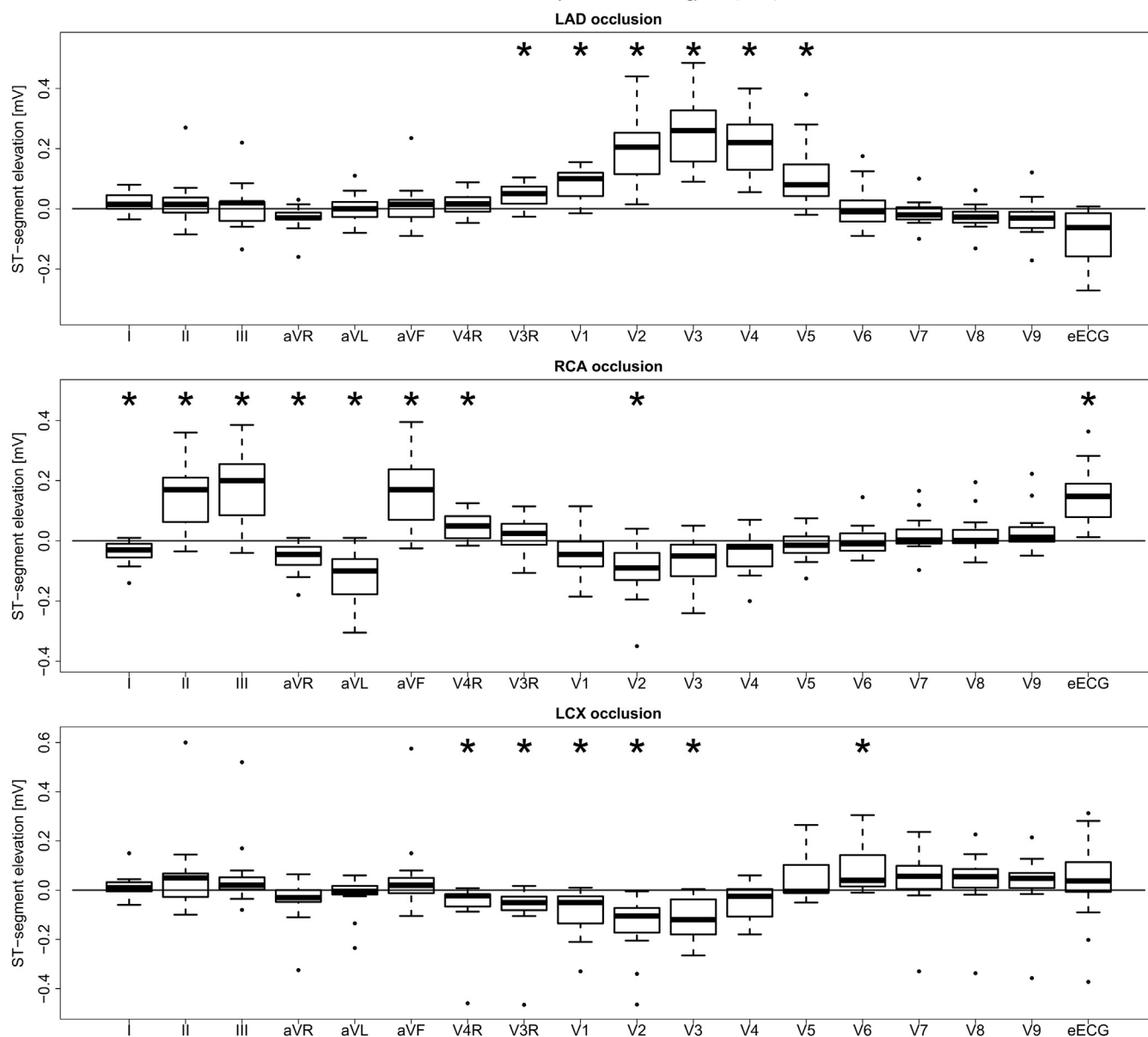


Fig. 1. ST-segment amplitude shifts after 60-second balloon occlusion. ST-segment shift (mV) is shown for the LAD (top panel), the RCA (middle panel) and the LCX territory (bottom panel). ST-segment shifts were statistically significant in leads highlighted with an asterisk (*).

[CI 0.65–0.9], Fig. 3, middle panel). Similarly, lead III showed 81% sensitivity and 68% specificity (AUC 0.77 [CI 0.65–0.89]). In contrast, specificity of the eECG was 85% but sensitivity only 50% (AUC 0.69 [CI 0.55–0.84]). ROC analysis showed that ST-segment elevation of 0.1 mV in the intracoronary ECG was best detected in the eECG at a cut-off value of 0.113 mV (specificity 85%, sensitivity 50%).

Detection of ischemia in the LCX territory

Median intracoronary ST-segment elevation was 0.56 mV (IQR 0.18–1.1 mV). In the other leads, median ST-segment elevation was most pronounced in lead V6 (0.04 mV [IQR 0.02–0.14 mV]), ST-segment depression was most pronounced in V1 (−0.05 mV [IQR −0.14 to 0.03 mV]), V2 (−0.11 mV [IQR −0.17 to 0.07 mV]) and V3 (−0.12 mV [IQR −0.18 to 0.04 mV]). ST-segment shifts were statistically significant in V4R, V3R, V1–V3 and V6 (all $p \leq 0.008$, Fig. 1, bottom panel).

Sensitivity and specificity to detect ischemia in the LCX territory were 26% and 100% for V2 (AUC 0.77 [CI 0.65–0.88]), 29% and 92% for V3 (AUC 0.69 [CI 0.56–0.83]) and 31% and 92% for V6 (AUC 0.69 [CI 0.55–0.82]), respectively (Fig. 3, bottom panel). Lead V2 outperformed I, III, aVL, V4 and V5 (all $p < 0.05$). After correction for multiple testing, V2 outperformed only lead aVL ($p = 0.041$). If an ST-segment elevation of 0.05 mV in V6 would have been considered to be indicative for ischemia (instead of 0.1 mV according to the AHA/ACCF/HRS recommendations), sensitivity and specificity of V6 would be 63% (CI 46%–77%) and 72% (CI 56%–88%), respectively.

Detection of ischemia in any territory

Retrospectively, the most dedicated three-lead combination to detect myocardial ischemia in any territory was V3, aVF and V6 (Fig. 4). This lead combination was able to detect ischemia with a sensitivity/specificity of 90%/75%

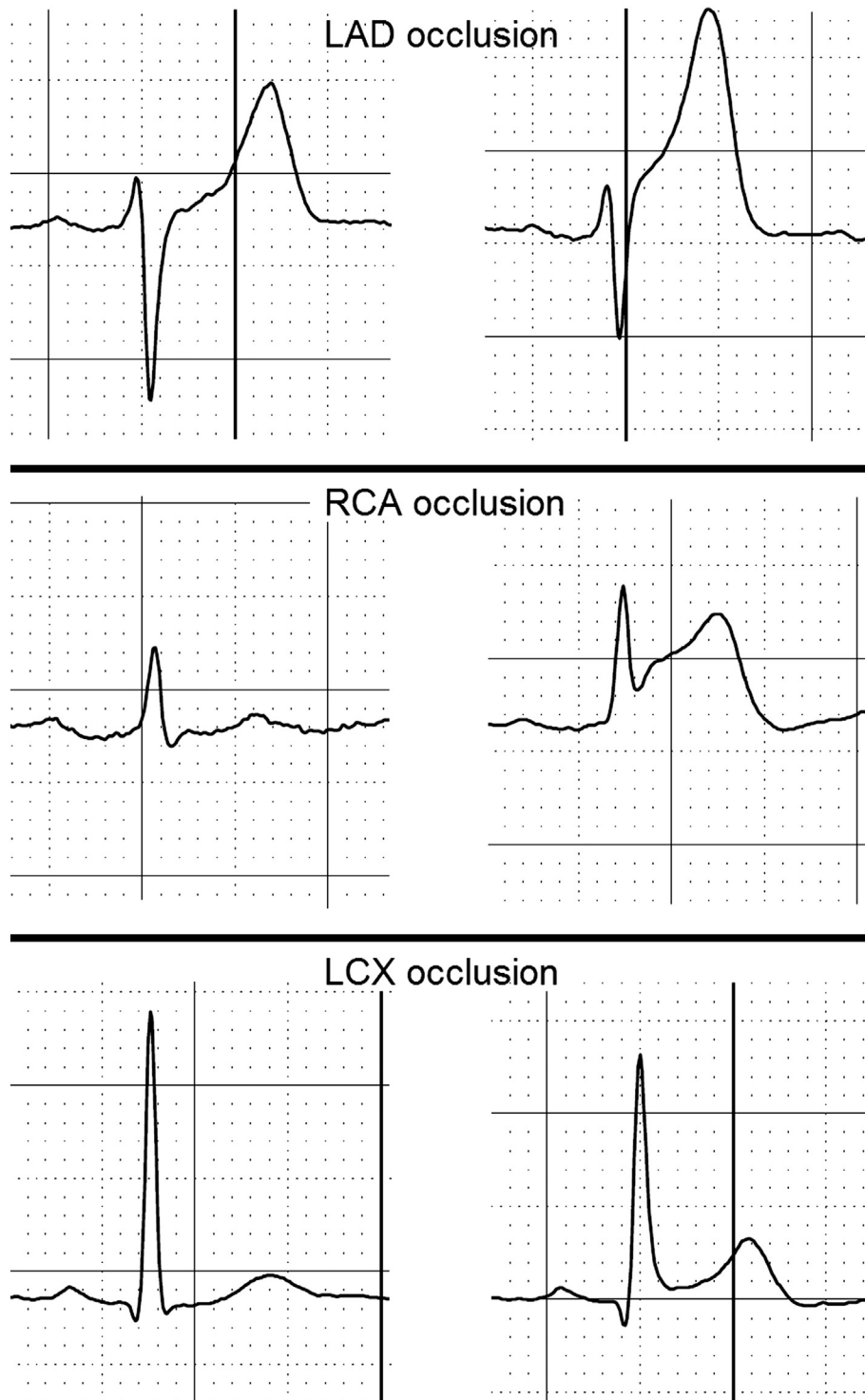


Fig. 2. Representative ECG samples immediately before (left column) and after 60 seconds (right column) of coronary occlusion. The top panel shows lead V3 during LAD occlusion, the middle panel lead aVF during RCA occlusion, the bottom panel lead V6 during LCX occlusion.

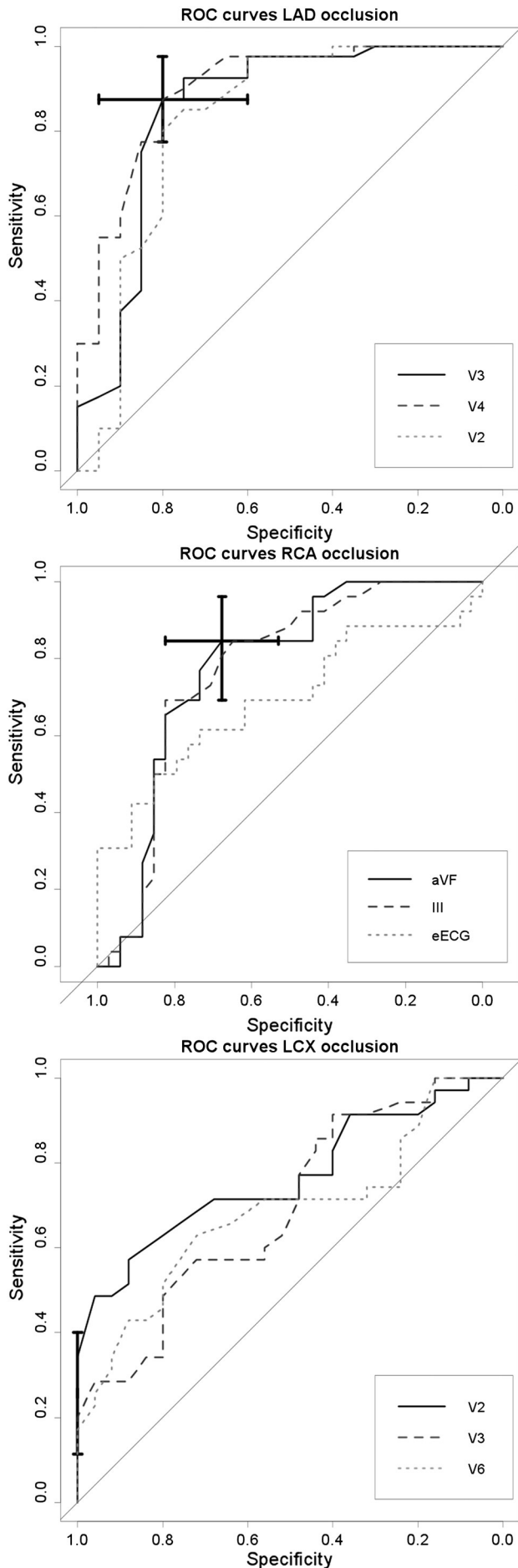
(LAD territory), 88%/53% (RCA territory) and 69%/60% (LCX territory). This lead configuration still needs six electrodes/cables placed onto the patient.

To minimize the number of electrodes even more, a bipolar lead combination should be chosen. The combination II/III shows the same performance as I/II/III and only needs four electrodes. The bipolar configuration shows a sensitivity/specificity of 10%/95% (LAD territory), 85%/68% (RCA territory) and 31%/80% (LCX territory, Fig. 4).

In contrast, the standard 12-lead ECG shows a better performance for ischemia detection, in particular a high sensitivity (98%/70% for the LAD territory, 88%/56% for the RCA territory, 74%/52% for the LCX territory, Fig. 4).

Correlation of collateral flow index and ST-segment shifts

We observed an inverse correlation of ST-segment shifts in the icECG and the CFI ($r_{\text{Spearman}} = -0.08$). Correlation of



ST-segment shifts in V3 and CFI during LAD occlusion was $r_{\text{Spearman}} = -0.22$. During LCX occlusion, correlation of ST-segment shifts and CFI was $r_{\text{Spearman}} = 0.14$ in V2 and $r_{\text{Spearman}} = -0.35$ in V6. During RCA occlusion, correlation of ST-segment shift and CFI was $r_{\text{Spearman}} = -0.41$ in the eECG and $r_{\text{Spearman}} = -0.12$ in aVF. None of these correlations were statistically significant.

Discussion

We present—for the first time—detailed quantitative experimental data on sensitivity and specificity of different ECG leads including an intracoronary and esophageal lead to detect myocardial ischemia.

Ischemia in the LAD territory is detected most reliably by precordial leads, RCA ischemia by the inferior leads and the eECG. To increase the poor sensitivity of the surface ECG to detect LCX ischemia, an adjusted ischemia threshold for V6 may be useful.

ST-segment shifts during balloon occlusion

There were no differences between the three patient groups (Tables 1 and 2) with respect to ST-segment shifts. However, three patients in the LCX group and four patients in the RCA did not develop ischemia (ST-segment elevation ≥ 0.1 mV in the intracoronary lead, Table 2) during balloon occlusion. The intracoronary lead has shown to be a highly sensitive tool for ischemia detection [13,17]. Thus, we assume that the balloon occlusion in these patients was not associated with significant ischemia due to several reasons. First, non-occlusive balloon inflation was seen on the fluoroscopy images in one patient. Second, left-dominant coronary circulation in the RCA group ($n = 2$) or right-dominant circulation in the LCX group ($n = 1$) may have prevented ischemia in a large myocardial area. In addition, CFI in the “non-ischemic” patients was slightly higher while balloon inflation pressure was lower (both not significant).

Detection of ischemia in the LAD territory

Ischemia in the LAD territory was best detected by the precordial leads V2–V4 (Figs. 1 and 3, top panel). ST-segment elevation was most pronounced in V3, as was already reported by Bush et al. [8]. V3 also showed the highest sensitivity and specificity for ischemia detection in the LAD territory (88% and 80%). However, no author has prospectively investigated the specificity of the precordial leads for ischemia detection using the icECG as gold standard for ischemia.

According to the AHA/ACCF/HRS [15], a ST-segment elevation of 0.2 mV (for men aged 40 or older) is considered to be indicative for ischemia in lead V3. We found both, sensitivity and specificity of V3 to be maximal at this cut-off value. Our findings provide additional evidence—also with

Fig. 3. Receiver operating characteristic analysis for the different occlusion territories (top panel: LAD, middle panel: RCA, bottom panel: LCX). Only the three leads with the largest ST-segment shift are shown. Confidence intervals for the best lead are shown for the AHA/ACCF/HRS threshold.

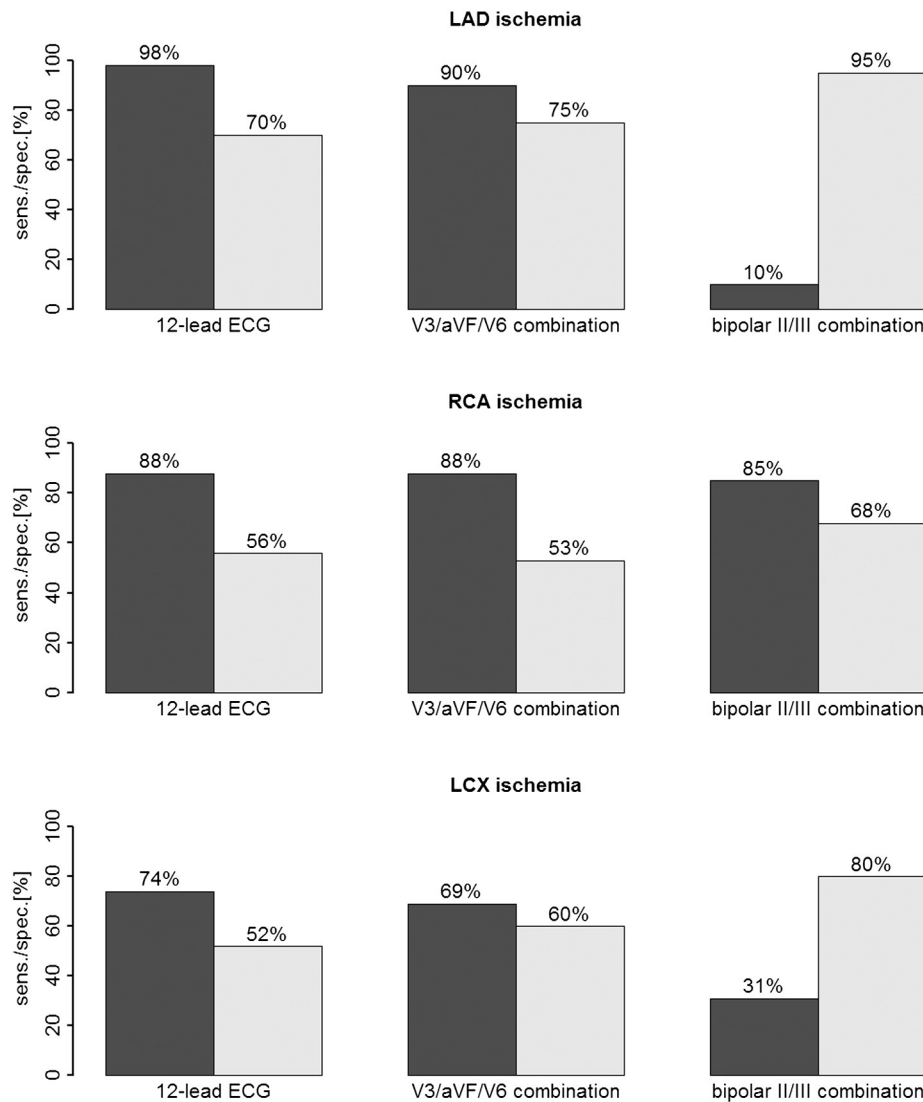


Fig. 4. Sensitivity (dark grey)/specificity (light grey) of the 12-lead ECG, the best 3-lead combination and the best bipolar lead configuration to detect ischemia (top panel: LAD, middle panel: RCA, bottom panel: LCX).

respect to optimal specificity for ischemia detection—that the AHA/ACCF/HRS recommendations propose ideal cut-off values for ischemia detection.

Detection of ischemia in the RCA territory

Ischemia in the RCA territory was best detected by the inferior leads and the eECG (Fig. 1 and 3, middle panel). Sensitivity was high in lead aVF (85%) and lead III (81%). A similar sensitivity has been reported by Zimetbaum et al. [18]. However, no prospective data concerning specificity of the surface ECG leads by using the icECG as a reference were published so far. According to our data, specificity of the inferior leads seems to be moderate. In contrast, the eECG shows a better specificity (85%) and exhibits a ST-segment elevation similar to lead II, III and aVF (Fig. 1, middle panel).

In past, conflicting data about the value of the eECG for ischemia detection have been published [19,20]. Jain [19] concluded that ST-segment changes in eECG during cardiac surgery may not be suitable for the detection of ischemia, since artifacts impair ST-segment analysis. In contrast,

Mittal et al. [20] considered the eECG to be helpful for the detection of postero-basal myocardial ischemia. We agree with Jain, that artifacts in the eECG may impede signal analysis. Though, a simple signal averaging algorithm—as used in this study—attenuates artifacts considerably without affecting systematically the ST-segment amplitude. However, it may be difficult to record an eECG in restless patients due to practical reasons.

Detection of ischemia in the LCX territory

ST-segment shifts during ischemia in the LCX territory were most pronounced in V1–V3 and V6, which corresponds with the findings of Wung and Drew [11] and Shah et al. [21]. Using the AHA/ACCF/HRS recommendations [15], we observed a poor sensitivity ($\leq 31\%$) of lead V2, V3 and V6. In contrast, specificity was $\geq 92\%$ in these leads. Our findings are confirmed by previous data, reporting that ischemia in the LCX territory is difficult to detect since 38%–47% of patients do not show ST-segment shifts in any standard ECG lead [11,22,23].

According to the ROC analysis, the AHA/ACCF/HRS thresholds were not optimal for detection of ischemia in the LCX territory. Based on our data, ST-elevation of 0.05 mV in lead V6 (instead of 0.1 mV) should already be indicative for ischemia in the LCX territory. This modified cut-off would increase sensitivity of V6 for LCX ischemia to 63% and specificity to 72%. Our proposition is supported by data presented by Macfarlane [24], who retrospectively published observational data on healthy subjects. From these data, it can be seen that healthy individuals only rarely exhibit ST-elevations >0.05 mV in lead V6. Thus, if ST elevation ≥ 0.05 mV in V6 would already be considered as a sign for ischemia, false positive findings would still be rare. Such an adapted threshold, however, would increase the sensitivity of lead V6 considerably. As an alternative method, more sophisticated visualization techniques like computed electrocardiographic imaging (CEI) may also improve ischemia detection [25]. In particular for LCX occlusions, visual assessment of CEI may be a useful tool to increase ischemia sensitivity.

Detection of ischemia in any territory

Using just a three-lead combination, the retrospective analysis showed that myocardial ischemia in any territory was most reliably detected by leads V3, aVF and V6. Based on a small patient population, Drew and Tisdale [7] have published data of different dual-, triple- and quadruple-lead combinations several years ago. None of these 82 lead combinations showed a higher sensitivity than the combination we suggest. Currently, ST-segment monitoring is mostly performed by recording a reduced lead system (V3, III or aVF and V5) [4]. It is important to point out, that these recommendations base on trials which did not evaluate “ischemic episodes” with an icECG as a reference for true ischemia and, thus, were not able to report data on specificity. However, high specificity is crucial for ST-segment monitoring in order to avoid false-positive alarms [1]. V3, aVF and V6 detect ischemia in any territory with high sensitivity and specificity, and, thus, may indicate the need to register a 12-lead ECG to confirm the suspected ischemia.

The sensitivity of our retrospectively proposed optimal three-lead combination is slightly smaller than the one of the “full picture” provided by the 12-lead ECG (Fig. 4). A further reduction in the number of ECG electrodes and cables is feasible if using only bipolar leads (no Wilson central terminal). A combination of standard bipolar leads, however, shows an extremely poor performance for ischemia in the LAD and LCX territory, due to the lack of precordial leads (Fig. 4). Thus, standard bipolar lead combinations do not provide reliable information regarding transient ischemic events. However, based on body-surface mapping studies during coronary occlusion, other alternative bipolar leads with optimized performance have been suggested [26]. We did not evaluate the performance of these leads in our study, but they may allow reducing further the number of electrodes/cables for ST-segment monitoring.

Collateral flow and ST-segment shifts

It has been shown that ST-segment shifts in icECG correlate inversely with CFI in the LAD, RCA and LCX territory [27]. Our data are in line with this trend, although we missed significance. The correlation of collateral flow and ST-segment shifts in surface ECG leads has not been investigated in detail [27]. An inverse correlation may also be found for the leads exhibiting ST-segment elevation during ischemia (e. g. V3 during LAD occlusion, V6 during LCX occlusion or aVF and eECG during RCA occlusion). Descriptive correlation analysis of our data was concordant to this hypothesis. However, most likely due to the small study population, we missed significance.

Limitations

Our study based on a population of 45 patients. Due to the limited patient number, performance differences between the ECG leads may have been missed. Due to the signal averaging, very short-lasting ST-segment shifts occurring within a few heartbeats only may not be detected. Thus, short transient ST elevations (e. g. due to coronary spasms) could be missed using our approach. Furthermore, ST-segment shifts were measured at the j-point. Measurements 40–80 ms after the j-point may have produced different results. In addition, coronary occlusions beyond 60 seconds may have produced a more pronounced ischemia, since ST-segment shifts asymptotically converge to a maximum [13]. Due to ethical reasons, we did not prolong the occlusion period. However, even for prolonged coronary occlusion, sensitivity of the standard ECG has been reported to be similar to our results [28] because ST-segment shifts reach their maximum very soon in the time course.

To induce ischemia, we always occluded the proximal part of the coronary artery. A more distal occlusion site may have produced a smaller/different ischemic area. Moreover, collateral flow, coronary anatomy and the percentage of occlusion affect the extent of ST-segment shift. Thus, our performance calculations have to be interpreted cautiously for a different patient population or situation (e.g. different coronary anatomy) and our results may then not have the same validity.

Finally, the reduced three-lead combination we propose is based on the retrospective selection of the best performing leads. This may have led to an overestimation of the three-lead ECG performance. Thus, these data may only serve as a basis for future prospective evaluation of this 3-lead combination vs. the standard 12-lead ECG.

Conclusion

In a well-controlled experimental setting in humans, we unveiled detailed data on sensitivity and specificity of different ECG leads to detect acute transient myocardial ischemia.

Ischemia in the LAD territory is detected best by leads V2–V4. During RCA occlusion, the most pronounced ST-segment shifts were observed in the inferior leads and the esophageal ECG. Sensitivity of the ECG to detect ischemia

in the LCX territory is poor. Lead V6 may be of use; however, this may require an adjustment of the AHA/ACCF/HRS recommendations for the interpretation of the ECG.

References

- [1] Drew BJ, Califf RM, Funk M, Kaufman ES, Krucoff MW, Laks MM, et al. Practice standards for electrocardiographic monitoring in hospital settings: an American Heart Association Scientific Statement From the Councils on Cardiovascular Nursing, Clinical Cardiology, and Cardiovascular Disease in the Young; endorsed by the International Society of Computerized Electrocardiology and the American Association of Critical-Care Nurses. *Circulation* 2004;110:2721–46.
- [2] Kawahito S, Kitahata H, Tanaka K, Nozaki J, Oshita S. Dynamic QRS-complex and ST-segment monitoring by continuous vectorcardiography during carotid endarterectomy. *Br J Anaesth* 2003;90:142–7.
- [3] Akkerhuis KM, Klootwijk PA, Lindeboom W, Umans VA, Meij S, Kint PP, et al. Recurrent ischaemia during continuous multilead ST-segment monitoring identifies patients with acute coronary syndromes at high risk of adverse cardiac events; meta-analysis of three studies involving 995 patients. *Eur Heart J* 2001;22:1997–2006.
- [4] Drew BJ, Krucoff MW. Multilead ST-segment monitoring in patients with acute coronary syndromes: a consensus statement for healthcare professionals. ST - segment monitoring practice guideline international working group. *American Journal of Critical Care: an official publication. Am Assoc Crit-Care Nurses* 1999;8:372–86 [quiz 387–378].
- [5] Klootwijk P, Meij S, von Es GA, Muller EJ, Umans VA, Lenderink T, et al. Comparison of usefulness of computer assisted continuous 48-h 3-lead with 12-lead ECG ischaemia monitoring for detection and quantitation of ischaemia in patients with unstable angina. *Eur Heart J* 1997;18:931–40.
- [6] Krucoff M. Identification of high-risk patients with silent myocardial ischemia after percutaneous transluminal coronary angioplasty by multilead monitoring. *Am J Cardiol* 1988;61:29F–35F.
- [7] Drew BJ, Tisdale LA. ST segment monitoring for coronary artery reocclusion following thrombolytic therapy and coronary angioplasty: identification of optimal bedside monitoring leads. *Am J Crit Care* 1993;2:280–92.
- [8] Bush HS, Ferguson 3rd JJ, Angelini P, Willerson JT. Twelve-lead electrocardiographic evaluation of ischemia during percutaneous transluminal coronary angioplasty and its correlation with acute reocclusion. *Am Heart J* 1991;121:1591–9.
- [9] Booker KJ, Holm K, Drew BJ, Lanuza DM, Hicks FD, Carrigan T, et al. Frequency and outcomes of transient myocardial ischemia in critically ill adults admitted for noncardiac conditions. *Am J Crit Care* 2003;12:508–16 [discussion 517].
- [10] Frazier SK, Brom H, Widener J, Pender L, Stone KS, Moser DK. Prevalence of myocardial ischemia during mechanical ventilation and weaning and its effects on weaning success. *Heart Lung* 2006;35:363–73.
- [11] Wung SF, Drew B. Comparison of 18-lead ECG and selected body surface potential mapping leads in determining maximally deviated ST lead and efficacy in detecting acute myocardial ischemia during coronary occlusion. *J Electrocardiol* 1999;32(Suppl):30–7.
- [12] Traupe T, Gloekler S, de Marchi SF, Werner GS, Seiler C. Assessment of the human coronary collateral circulation. *Circulation* 2010;122:1210–20.
- [13] Friedman PL, Shook TL, Kirshenbaum JM, Selwyn AP, Ganz P. Value of the intracoronary electrocardiogram to monitor myocardial ischemia during percutaneous transluminal coronary angioplasty. *Circulation* 1986;74:330–9.
- [14] Krasteva V, Jekova I. Qrs template matching for recognition of ventricular ectopic beats. *Ann Biomed Eng* 2007;35:2065–76.
- [15] Wagner GS, Macfarlane P, Wellens H, Josephson M, Gorgels A, Mirvis DM, et al. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part VI: acute ischemia/infarction: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society; endorsed by the International Society for Computerized Electrocardiology. *Circulation* 2009;119:e262–70.
- [16] R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. 2013. <http://www.R-project.org>.
- [17] Fischell TA, Fischell DR, Fischell RE, Baskerville S, Hendrick S, Moshier C, et al. Potential of an intracardiac electrogram for the rapid detection of coronary artery occlusion. *Cardiovasc Revasc Med* 2005;6:14–20.
- [18] Zimetbaum PJ, Krishnan S, Gold A, Carrozza II JP, Josephson ME. Usefulness of ST-segment elevation in lead iii exceeding that of lead ii for identifying the location of the totally occluded coronary artery in inferior wall myocardial infarction. *Am J Cardiol* 1998;81:918–9.
- [19] Jain U. Wave recognition and use of the intraoperative unipolar esophageal electrocardiogram. *J Clin Anesth* 1997;9:487–92.
- [20] Mittal SR, Sethi JP, Sharma D. The role of esophageal leads in the detection of exercise-induced postero-basal ischemia. *Int J Cardiol* 1989;23:69–77.
- [21] Shah A, Wagner GS, Green CL, Crater SW, Sawchak ST, Wildermann NM, et al. Electrocardiographic differentiation of the ST-segment depression of acute myocardial injury due to the left circumflex artery occlusion from that of myocardial ischemia of nonocclusive etiologies. *Am J Cardiol* 1997;80:512–3.
- [22] Berry C, Zalewski A, Kovach R, Savage M, Goldberg S. Surface electrocardiogram in the detection of transmural myocardial ischemia during coronary artery occlusion. *Am J Cardiol* 1989;63:21–6.
- [23] Huey BL, Beller GA, Kaiser DL, Gibson RS. A comprehensive analysis of myocardial infarction due to left circumflex artery occlusion: comparison with infarction due to right coronary artery and left anterior descending artery occlusion. *J Am Coll Cardiol* 1988;12:1156–66.
- [24] Macfarlane PW. Age, sex, and the st amplitude in health and disease. *J Electrocardiol* 2001;34(Suppl):235–41.
- [25] Akil S, Al-Mashat M, Heden B, Hedeer F, Jogi J, Wang JJ, et al. Discrimination of st deviation caused by acute coronary occlusion from normal variants and other abnormal conditions, using computed electrocardiographic imaging based on 12-lead ECG. *J Electrocardiol* 2013;46:197–203.
- [26] Horacek BM, Wagner GS. Electrocardiographic ST-segment changes during acute myocardial ischemia. *Cardiac Electrophysiol Rev* 2002;6:196–203.
- [27] de Marchi SF, Streuli S, Haefeli P, Gloekler S, Traupe T, Warncke C, et al. Determinants of prognostically relevant intracoronary electrocardiogram ST-segment shift during coronary balloon occlusion. *Am J Cardiol* 2012;110:1234–9.
- [28] Pettersson J, Pahlm O, Carro E, Edenbrandt L, Ringborn M, Sommo L, et al. Changes in high-frequency qrs components are more sensitive than ST-segment deviation for detecting acute coronary artery occlusion. *J Am Coll Cardiol* 2000;36:1827–34.